Thymoma (Case Report): Importance of Comorbidity, Lifestyle, and Thymoma Size in Treatment Success

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Abstract

Background: Thymoma is a rare malignancy with an incidence of 0,15 case per 100.000 population and is the most commonly diagnosed anterior mediastinal malignancy. With 12,5% 15-year survival rate, and is often accompanied by autoimmune disease such as myasthenia gravis, pure red blood cell aplasia, and hypogammaglobulinemia, better understanding of factors affecting prognosis is needed to improve patient quality of life and survival.

Case: We presented two cases in this study, a 33-year-old woman and a 31-year-old man, both had the main complaint of worsening shortness of breath unrelated to activity. The second patient was a smoker, alcoholic, obese, and hypertensive. Physical examination in both patients showed dullness and decreased breath sound in the affected side of the lungs. Chest x-ray and subsequent chest CT showed mediastinal widening. USG-guided FNAB suggested thymoma as one of the possible pre-surgery diagnoses, and later tissue pathological analysis after median sternotomy and mass debulking in both patients confirmed the diagnosis, with a larger tumor size in second case-patient compared to the first case. In the first case, the patient was allowed for outpatient treatment few days after surgery, and underwent first-line chemotherapy with carboplatin-etoposide, with subsequent CT RECIST showing progressive disease. Patient then rejected surgery recommendation and preferred to continue chemotherapy. Chemotherapy then continued with paclitaxel and showed progressive disease after 3 series of chemotherapy. The patient rejected surgery recommendation again and preferred to continue chemotherapy. Chemotherapy continued with gemsitabin. Patient had several complications such as pneumonia and heart failure and died with respiratory failure. In the second case, patient did not respond well to surgery. Patient was diagnosed with respiratory failure on prolonged ventilator, pneumonia, and sepsis. Patient died with respiratory failure and sepsis.

Conclusion: In this study, two different thymoma cases with different lifestyle, comorbidity, and tumor size showed different treatment response. This finding, along with several findings in previous studies could be used to further validate smoking, alcohol consumption, hypertension, obesity, and tumor size as prognostic factors in thymoma

Keywords: Thymoma, Lifestyle, Comorbidity, Tumor size, Treatment response

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1. Introduction

Thymoma is a neoplasma of thymic origin commonly occurred in the anterior mediastinum. Thymoma is a rare malignancy with a yearly incidence of 0,15 case per 100.000 population and is the most commonly identified anterior mediastinal malignancy. 34% cases of thymoma is accompanied by autoimmune disease such as myasthenia gravis, pure red blood cell aplasia, and hypogammaglobulinemia[1,2]. With 15-year survival rate of 12,5% in invasive thymomas and 47% in noninvasive thymomas, a better understanding of various factors affecting treatment success in thymoma is needed to improve quality of life and survival[3].

In this case report, two cases of thymoma in 36 years old women and 31 years old men were reported. Both patients had differences in lifestyle, comorbidity, tumor size, and subsequent treatment outcomes. We discussed how comorbidity, lifestyle, and tumor size affect treatment outcome in patients with thymoma.

2. Case

Case 1

A 33-year-old woman complained of shortness of breath since 5 months ago, and had been worsening for the last 2 days. Shortness of breath did not worsen with activity and no complaint of nocturnal awakening caused by shortness of breath. The patient also complained about left chest pain described as 'being-stabbed' with Visual Acuity Score (VAS) 2, no radiation, no relation with activity, and no nausea or vomiting. Complaints of cough, fever, and palpitation were denied.

Patient had been diagnosed with mediastinal mass in Hermina Hospital in September 2020 and referred to dr. Saiful Anwar General Hospital for further examination. Patient has undergone chest x-ray, chest computed tomography (CT), ultrasonography (USG)-guided fine needle aspiration biopsy (FNAB), abdominal USG, and sputum cytological exam in January 2021.

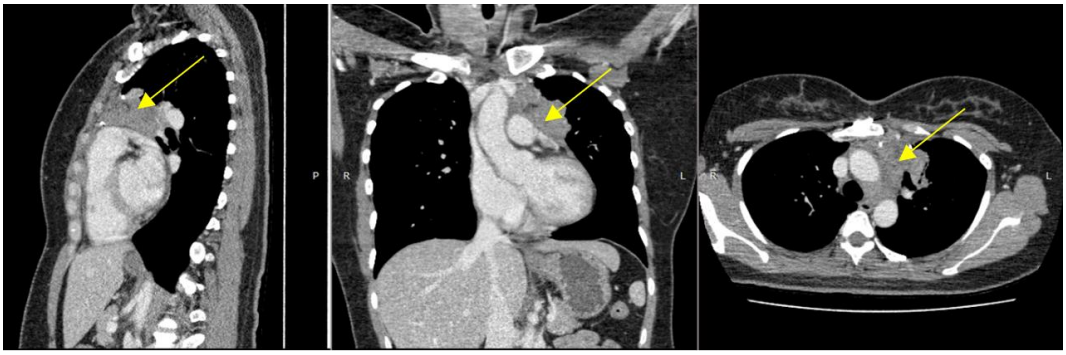

Figure 1. Chest CT examination in January 2021 showed solid mass in anterior mediastinum (arrow).

Physical examination showed moderately ill, alert patient with blood pressure of 100/70 mmHg, pulse rate of 86x/minute, respiratory rate of 20x/minute, and axillary temperature of 36ºC. Cardiac, abdominal, and extremities findings were normal. Lung inspection showed symmetrical static and dynamic breathing pattern. Dullness in percussion and decreased vesicular breathing were found in the left side of the lung.

Laboratory examination showed leukocytosis (13.100/uL [normal value 4.700-11.300]), decrease of hematocrite (36,9% [normal value 38-42]), decreased urea (16,1 mg/dL [normal value 16,6-48,5]), and increased C-reactive protein (CRP) (0,98 mg/dl [normal value < 0,3]). Pulmonary function examination showed mild restriction. Sputum cytology showed class II findings with epithelial inflammatory changes containing polymorphonuclear (PMN), mononuclear (MN), and histiocyte. No malignant cell detected.

Chest x-ray examination in September 2020 showed left mediastinal widening with mediastinal mass suspected. In March 2021, left mediastinal widening is still shown with bilateral fluidothorax and pulmonary congestion (Figure 1.1). Chest CT examination in January 2021 showed solid mass adhered to anterior wall of thorax, sternum, and surrounding great vessels (Figure 1.2). Multiple lymphadenopathies were found in prevascular and paratracheal area. Abdominal USG showed no abnormalities nor metastatic nodules. Anterior thorax USG-guided FNAB showed

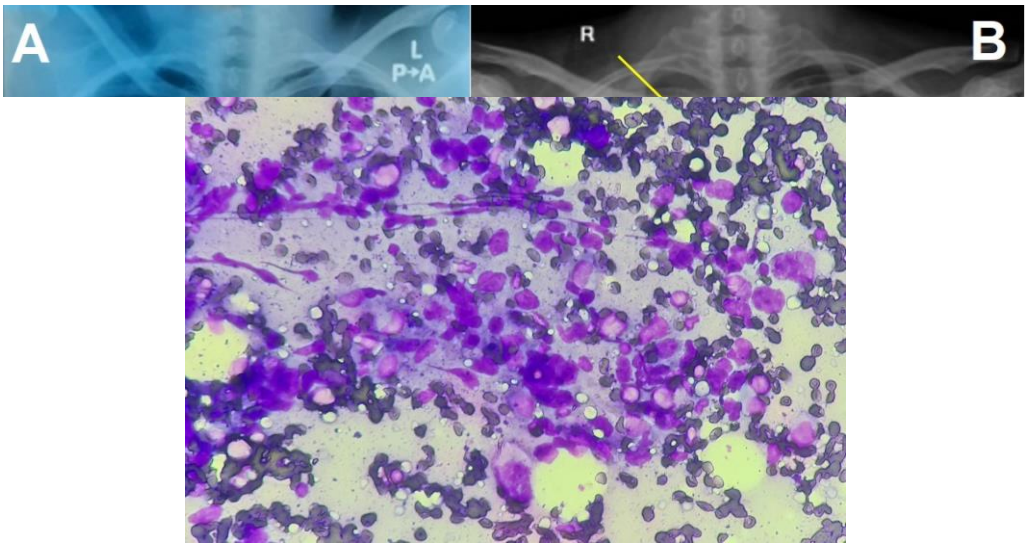

Figure 2. USG-guided FNAB showed polygonal tumor cells with nuclear fold and atypical mitosis (purple).

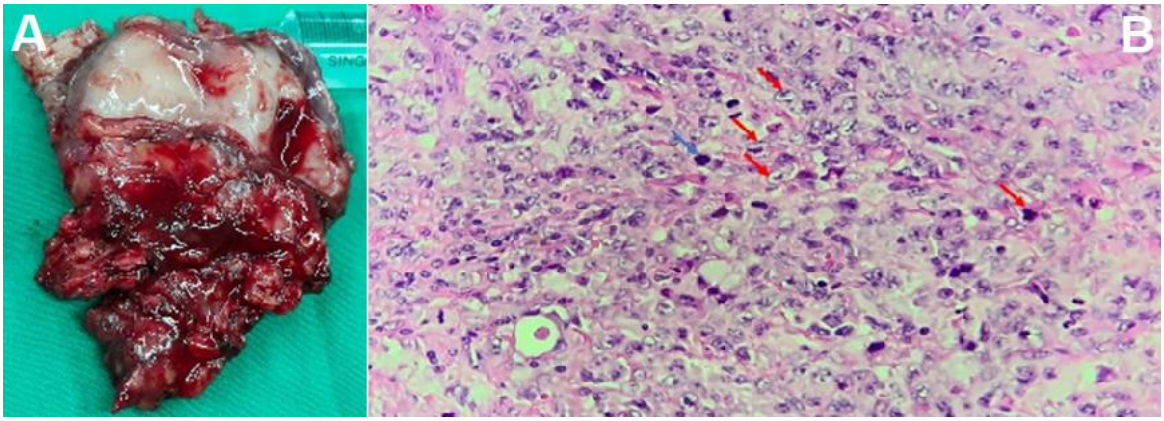

Figure 3. Macroscopic view of the resected mass (A). Microscopic pathological examination of tissue acquired in mass debulking showed polygonal cancer cells with round nuclei and nuclear fold (red arrow), with atypical mitosis (blue arrow), suggesting malignant round cell tumor thymoma B3 (B).

polygonal tumor cells with round nuclei, prominent eosinophilic cytoplasmic nuclei, and atypical mitosis (Figure 1.3). Patient then diagnosed with mediastinal tumor and thymoma as the suspected etiology.

Patient underwent median sternotomy and mass debulking surgery in March 2021. An anterior mediastinal mass was found adhered to pericardium and upper left lobe of the lung and was able to be freed. Tissue samples were taken for pathological examination. Macroscopic examination showed a 10 x 6 x 3 cm mass. Microscopic pathological examination showed malignant tissue separated by connective tissue. Polygonal tumor cells with round nuclei and nuclear fold. Atypical mitosis were identified, suggesting malignant round cell tumor thymoma B3 (Figure 1.4).

Postoperative laboratory examination showed hypokalemia (3,47 mEq/L [normal value 3,5-5.0]), hyperchloremia (109 mEq/L [normal value 98-106]), shortened activated partial thromboplastin time (APTT) (24s [normal value 24,6-30,6]), and hypoalbuminemia (3,42 g/dL [normal value 3,5-5,5]). Postoperative chest x-ray showed left mediastinal widening, pulmonary congestion, and left fluidothorax (Figure 1.5).

After the surgery was done and diagnosis of thymoma confirmed, first line chemotherapy was initiated with 700 mg carboplatin and 160 mg etoposid regimen. After 3 series of chemotheraphy, a response evaluation criteria in solid tumors (RECIST) CT scan was done in June 2021 with stable disease in target lesion and new lesion (-) (Figure 1.6). Chemotherapy regimen was continued for 2 further series and subsequent RECIST CT scan was done in September 2021, showing overall progressive disease.

Following CT result, mass debulking and thymectomy were suggested, but rejected by the patient. Patient preferred to continue second line chemotherapy regimen with Paclitaxel. After 3 series of chemotherapy with Paclitaxel, CT RECIST was done in December 2021 and showed partial response in target lesion, progressive disease in non target lesion, new lesion (+) with an overall response of progressive disease (Figure 1.7). Mass debulking and thymectomy were still suggested, but the patient rejected and prefer to continue to third line chemotherapy regimen with gemsitabin.

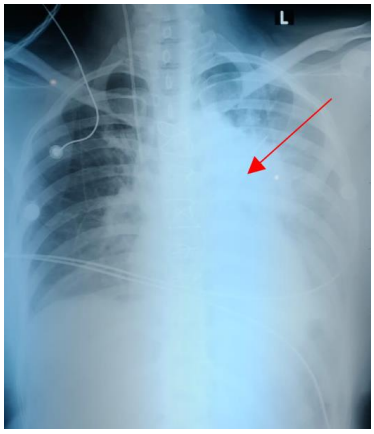

Figure 1.5. Postoperative chest x-ray examination showed left mediastinal widening, pulmonary congestion, and left fluidothorax.

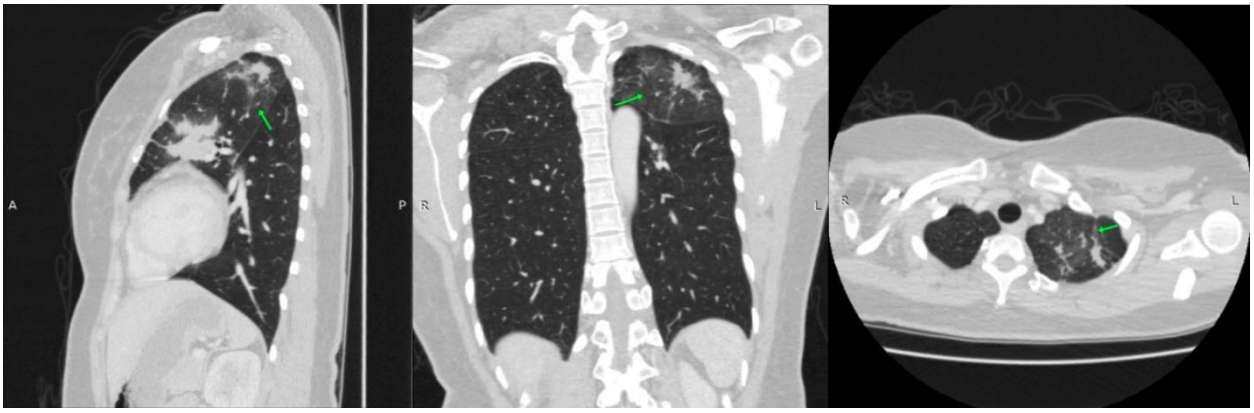

Figure 1.6. CT RECIST examination in June 2021 showed left anterior mediastinal mass covering great vessel and adhering to anterior thorax wall (arrow), multiple mediastinal lymphadenopathies, ground glass opacity, and left lung fibrosis.

In the process of this third line chemotherapy, some complication arised such as pneumonia, bilateral pleural effusion, insomnia, anxiety, heart failure, and grade II vena cava superior syndrome (VCSS). night awakening caused by shortness of breath. Patient also complained about productive cough with whitish expectorant. Chest pain, fever, and palpitation were denied. Patient has a history of uncontrolled

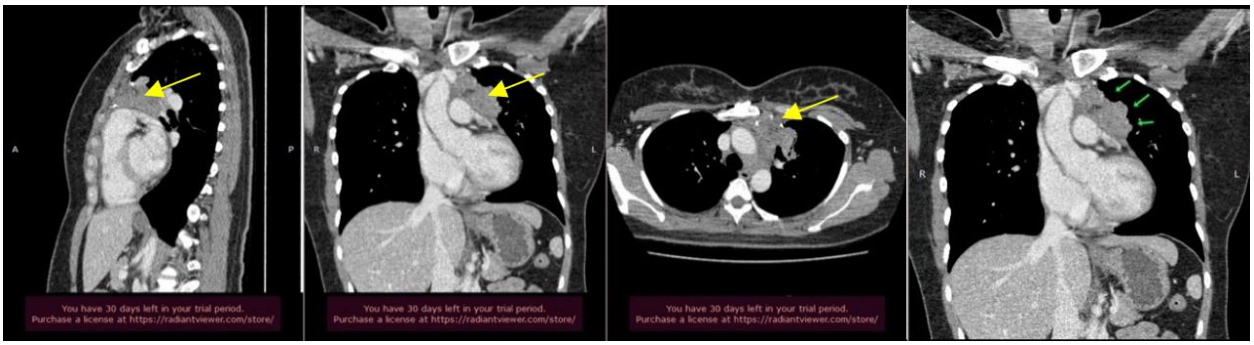

Figure 1.7. CT RECIST in December 2021 showed expanding anterior and middle mediastinal mass with overall response of progressive disease.

Subsequent palliative 5.0 Gy radiotherapy were done for 5 times. Patient died in February 2022 with respiratory failure.

Case 2

A 31-year-old man complained of shortness of breath felt since 1 month ago and worsened in the last 3 days. Shortness of breath did not worsen with activity and no hypertension, is an active smoker and routinely consumes alcohol.

Patient had been diagnosed with mediastinal mass and thymoma as the suspected etiology at Hermina Hospital in February 2021. Patient then referred to dr. Saiful Anwar General Hospital for further examination. Patient had undergone chest x-

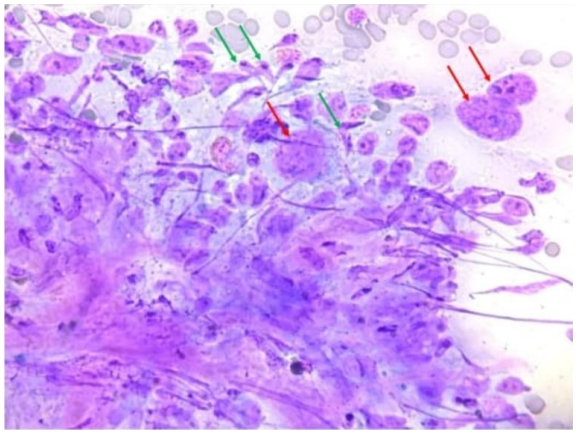

Figure 2.1. Microscopic examination of USG-guided FNAB showed circular (red arrow) and spindle (green arrow) cells with pleomorphic nuclei, suggested thymoma finding.

ray and CT scan examination in February 2021, and USG-guided FNAB examination in March 2021 before referred.

Physical examination showed moderately ill, alert patient with blood pressure of 120/80 mmHg, pulse rate of 80x/minute, respiratory rate of 20x/minute and axillary temperature of 36,8^{o}C. Patient is obese with BMI of 32,9. Heart, abdominal, and extremities examination showed normal findings, while dullness in percussion at the left side and decreased vesicular breathing at the upper left side were found in lung examination.

Laboratory examination showed leukocytosis (17.800/UI [normal value 4.700-11.300]) and thrombocytosis (618.000/uL [normal value 142.000-424.000]). USG-guided FNAB showed circular and spindle cells with pleomorphic nuclei, suggested thymoma finding (Figure 2.1). Chest x-ray examination in February 2021 showed middle mediastinal mass with bronchitis and lung hyperinflation, while in March 2021 showed anterior mediastinal mass (Figure 2.2). Chest CT scan showed solid multilobulated mass in anterior, middle, and posterior mediastinum (Figure 2.3).

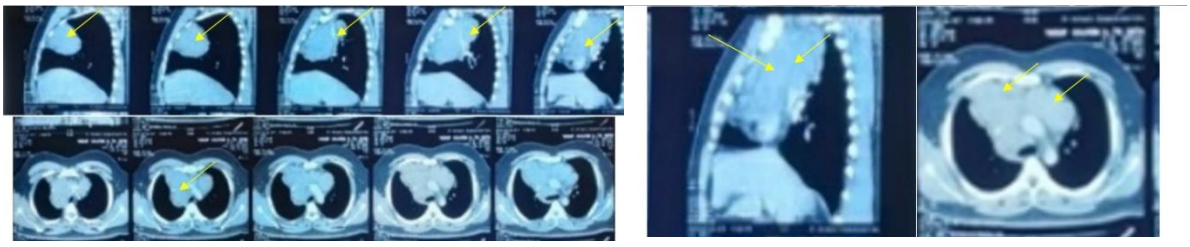

Figure 2 Figure 2.3. Chest CT examination in February 2021 showed solid mass suggesting conglomerated lymphadenopathies in anterior, middle, and posterior mediastinum with parts adhered to anterior thorax wall.

Patient then underwent sternotomy and mass debulking in April 2021. Mediastinal space examination showed tumor mass adhered to pericardium, enveloping aorta to medial lobe of right lung, suggesting thymoma. Mass debulking was done, with samples from the tumor and pericardium taken for pathological examination, which showed round tumor cells and surrounding sclerotic area (Figure 2.4).

Serial postoperative chest x-ray showed anterior mediastinal mass relatively similar in size with pneumonia, pulmonary infiltrate, pleural effusion, and subcutaneous emphysema (Figure 2.5). After surgery, patient is on prolonged ventilator use, and underwent thoracostomy and thoracic lavage on 14 April 2021. Bacterial culture examination showed multi drug resistant (MDR) *Acinobacter baumannii* and *Enterobacterium cloaca* in sputum, *Corynebacterium striatum* and *C. stenata* in pus, extended drug resistant (XDR) *Acinetobacter baumannii* in urine, *Aerococcus viridans* in drain, and *Candida tropicalis* in blood. Patient's condition kept deteriorating and patient died on 27 April 2021 with sepsis and respiratory failure.

Immunohistochemical analysis from pericardiac tumor tissue showed negative finding on CK staining, positive staining of CD45 in lymphoid cells, CD20 in B lymphocytes and large cells, CD30 in large cells, CD3 with rosetting in large cells, and Ki67 in 60% of tumor cells with strong intensity. This result showed grey zone lymphoma and CD30-positive diffuse large B cell lymphoma.

3. Discussion

In this study, 2 cases of thymoma involving a 33-year-old woman and 31-year-old man were reported. Epidemiologically, thymoma is rare among cancers, contributing to 1% of all adult malignancies. 47% of anterior mediastinal cancer and 15 – 21,7%

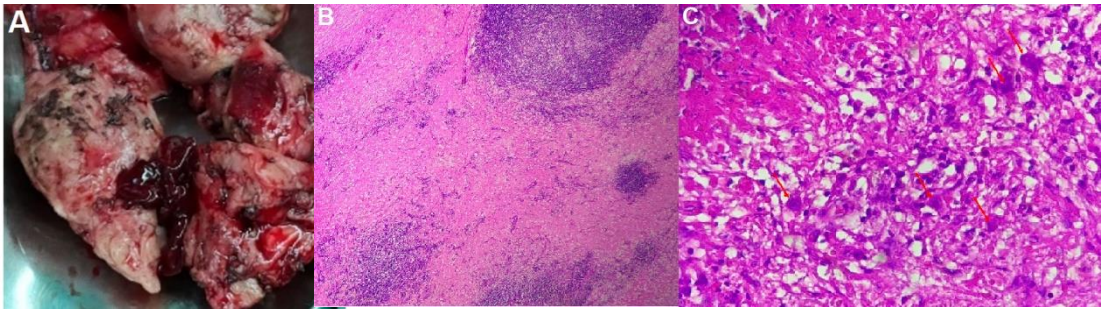

Figure 2.4. Macroscopic examination showed solid whitish-grey tumor tissues 11 x 6,5 x 2,5 cm and 4,5 x 2 x 0,5 cm in size (A). Microscopi examination showed tumor growth with sclerosing areas (B). Round, pleomorphic, hyperchromatic tumor cells with thin cytoplasma (arrow) and surrounding inflammatory eosinophils and histyocytes can be seen (C).

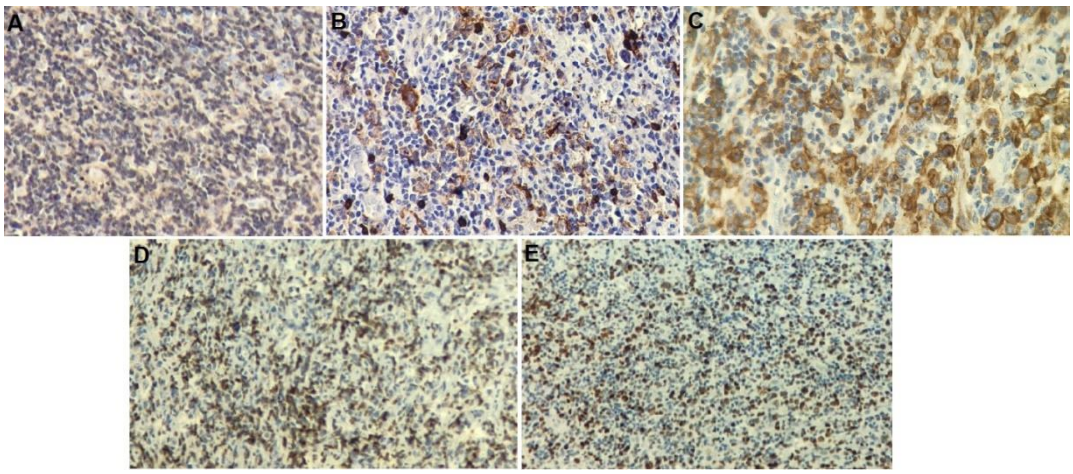

Figure 2.5 Immunohistochemical analysis showed positive staining on CD45 (A), CD20 (B), CD30 (C), CD3 (D), and Ki67 (E)

of all mediastinal cancer is thymoma. Although thymoma can occur at 7 to 89 years old with the highest incidence between 55 to 65 years, median age of diagnosis in thymoma patients is 33 years. No gender preference found in previous studies[2].

In both cases, the main complain is shortness of breath that did not worsen with activity. Accompanying symptom in the first case was left chest pain, and productive cough in the second case. Previous study showed that 40% thymoma cases are asymptomatic. In symptomatic case, the most commonly occuring local symptom is cough (60%). Obstructive symptoms such as shortness of breath, chest pain, hoarseness, and dysphagia are related to disease progress[4]. Large thymoma can compress surounding structures such as superior vena cava. Compression of this structure can result in superior vena cava syndrome, increasing intracranial venous pressure, resulting in periorbital, facial, and upper extremities edema. Large thymoma can also lead to ocular and sympathetic tract lesion, causing Horner syndrome with unilateral miosis, ptosis, and facial anhidrosis[5].

Factors that differ significantly between patients reported in this study is lifestyle and comorbidity. The second case patient consumed alcohol regularly and is a smoker. Previous study showed that 58,1% thymoma patients are smoker[6]. A multicenter, case-control study showed increasing risk of thymoma in smoker (OR 1.4) and heavy smoker($\geq$ 41 packs/year) (OR 2.1)[7]. A 2017 genetic study also showed that smoking is related to atleast 11 oncogenic pathways[8]. High alcohol consumption ($\geq$ 25 g alcohol/day) is associated with thymoma (OR 2.4)[7]. Genetic characterization study showed that alcoholism is the second most

associated signaling pathway related to thymoma[9].

Hypertension and obesity are comorbidities found in the second case patient. Thymoma is related to hypertension by alteration of thymus function caused by angiotensin II. Angiotensin II downregulates ATRAP expression, leading to alteration of thymus transcription factor Foxn1, causing T lymphocyte dysfunction and endothelial damage leading to hypertension[10]. Previous study by Xue et al. showed 29% of thymoma patients were hypertensive, while study by Samardžić et al. showed almost half (48,4%) of thymoma patients were hypertensive[6,11]. Obesity is known to accelerate thymic aging and fatty inflitration of thymus[12,13]. In thymoma patients, previous study showed that obese patients were related to significantly higher risk of complication (p=0,033) and postoperative respiratory failure (p=0,005)[14].

After chest x-ray examination, in both cases, patients underwent chest CT examination to confirm previous chest x-ray results. In the first case, solid mass with inside fatty part was found in anterior mediastinum, adhering to anterior thorax wall, sternum, and great vessels, suggesting teratoma, thymoma, or lymphoma. In the second case, solid, multilobulated mass conglomerated in anterior, middle, and posterior mediastinum was found, suggesting lymphadenopathy. Chest x-ray examination is recommended for early detection of thymoma, while chest CT with intravenous contrast is the most important evaluative assesment to visualize different tissues with different attenuations[15,16]. In both cases, USG-guided FNAB was done and showed suspected thymoma, with subsequent pathological analysis needed to confirm diagnosis. Diagnostic biopsy in thymoma can be done via transthoracal and transbronchial needle aspiration. Mediastinoscopy and video-assisted thoracoscopic surgery (VATS) are other options for diagnostic biopsy in thymoma[17–19].

Both patients then underwent median sternotomy and mass debulking surgery. In the first case, a 10 x 6 x 3 cm mass was found adhering to pericardium and upper left lobe of the lung. Pathologic analysis showed malignant round cell tumor suggesting thymoma B3. In the second case, tumor mass 11 x 6,5 x 2,5 cm and 4,5 x 2 x 0,5 cm in size was found adhering to pericardium, aorta, and middle right lobe of the lung. Pathological analysis showed round, pleomorphic tumor cells with sclerosing areas suggesting hodgkin lymphoma or thymic carcinoma. Previous study showed

that tumor size was significantly related to survival in thymoma (p<0,001). Tumor size also related to metastasis and therapeutic success, with large tumor size related to higher rate of metastasis (p<0,001), and in smaller tumors (<90 mm), chemotherapy is a significant negative predictive factor of survival (p<0,001)[20]. These findings are inline with both of our cases, with larger tumor (second case) responded poorly to treatment compared to the smaller sized tumor (first case). Although tumor size is not yet specifically considered as independent prognostic factor in thymoma, we hope that findings in this study could help in validating tumor size as prognostic factor in thymoma[21].

Few days after surgery, the first case patient was allowed for outpatient treatment. The patient underwent chemotherapy with carboplatin-etoposid regiment. In the second case, the patient was on prolonged ventilator use following surgery. Bacterial culture examination showed several MDR and XDR bacterias in patient's urine and sputum. Patient then diagnosed with hospital acquired pneumonia (HAP) post sternotomy + respiratory failure on prolonged ventilator + sepsis and died in the 29th day of treatment.

In the first case, after the third series of chemotherapy, CT RECIST showed stable disease and chemotherapy was continued until the fifth series, with the next CT RECIST showed progressive disease. Mass debulking and thymectomy were suggested but patient rejected and preferred to continue chemotherapy. After three series of second line chemotherapy (paclitaxel regiment), CT RECIST showed overall progressive disease. Mass debulking and thymectomy was suggested again but patient preferred to continue chemotherapy. Patient underwent third line chemotherapy with gemsitabin. Complications started to arise, such as pneumonia, bilateral pleural effusion, HF, and grade II VCSS. Palliative radiotherapy was done for 5 times, and patient died with respiratory failure. In operable thymoma, induction chemotherapy before surgery, followed by consolidation chemo and radiotherapy after surgery is associated with 5-year survival rate of 95%. Induction chemotherapy regiment consists of three cycle cyclophosphamide, doxorubicin, cisplatin, and prednison. Consolidation chemotherapy consists of the same cycle with dosage reduced to 80%. In advanced stage thymoma that is inoperable, regiment of choice for chemotherapy consists of cisplatin, vincristine, doxorubicin, and etoposide can result in mean survival period of 49 months[22].

However, in the second case, final immunohistochemical analysis showed

immunological findings confirming B cell lymphoma. Previous studies showed coexistence of thymoma and lymphoma[23,24], and difficulties to properly distinguish lymphoma and thymoma[25]. A 2022 case report study showed patient with cervical thymoma and arm B-cell lymphoma with subsequent myasthenia gravis. In this study, pathological difficulties of distinguishing between thymoma and B-cell lymphoma was highlighted, requiring high quality hematoxylin-eosin-stained histological section and careful histological evaluation. Previous immunostaining only done from arm tissue also contributed to early misdiagnosis (B-cell lymphoma only) in this study. However, myasthenic symptoms such as ptosis in this patient suggested thymoma, with subsequent cervical tissue immunostaining confirmed this additional diagnosis[23]. Myasthenia gravis is associated with thymoma, being found in 50% of classic thymoma cases[26].

Another case report showed T-cell lymphoma in right anterior mediastinum, previously diagnosed as type B1 thymoma 8 years prior, with patient declined surgery and lost to follow-up at that time. This finding confirmed previous findings in studies that showed thymoma with additional neoplasms[27,28]. Expression of CD45 and sCD3 can be useful in identifying thymoma against T-cell lymphoma. However, distinguishing thymoma and lymphoma, especially in similar mass location (such as anterior mediastinum) is clinically and pathologically challenging[24].

In both cases presented in this study, different outcomes were noted. First case patient responded the treatment better, compared to the second case patient. The second case patient had underlying comorbidity such as hypertension and obesity, as well as negative lifestyle such as smoking and alcohol consumption. Aside from lifestyle and comorbidity, the second case patient also had larger tumor size that could contribute to worse treatment response compared to the first case patient.

4. Conclusion

In this study, two cases of thymoma in a 33-year-old woman and 31-year-old man were reported. Diagnosis were based on history taking, physical examination, chest x-ray, chest CT, USG-guided FNAB, and tissue biopsy. Both patients had different lifestyle, comorbidity, and tumor size that could contribute to overall disease and treatment progression. Although underwent the same procedure (median sternotomy and mass debulking), second case patient which had bad lifestyle habits (smoking and alcohol

consumption), comorbidites (hypertension and obesity), and larger tumor size had worse treatment response. This finding could be used for further validation of lifestyle, comorbidity, and tumor size as prognostic factors in thymoma.

References

1. Mitchell RN, Kumar V, Abbas AK, Aster JC. Pocket companion to Robbins and Cotran pathologic basis of disease. Ninth edition. Philadelphia, PA: Elsevier; 2017.
2. Almeida PT, Heller D. Anterior Mediastinal Mass. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2022 Aug 1]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK546608/
3. Robinson SP, Akhondi H. Thymoma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2022 Aug 1]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK559291/
4. Friedman T, Quencer K, Kishore S, Winokur R, Madoff D. Malignant Venous Obstruction: Superior Vena Cava Syndrome and Beyond. Semin intervent Radiol. 2017 Dec;34(04):398–408.
5. Knyazer B, Smolar J, Lazar I, Rosenberg E, Tsumi E, Lifshitz T, et al. Iatrogenic Horner Syndrome: Etiology, Diagnosis and Outcomes. Isr Med Assoc J. 2017 Jan;19(1):34–8.
6. Samardzic N, Jovanovic D, Markovic-Denic L, Sarac S, Skodric-Trifunovic V, Stojsic J, et al. Clinicopathological retrospective analysis of thymoma in Serbia: Single center experience. VSP. 2020;77(2):140–50.
7. Eriksson M, Kaerlev L, Johansen P, Afonso N, Ahrens W, Costa-Pereira A, et al. Tobacco smoking and alcohol consumption as risk factors for thymoma - A European case-control study. Cancer Epidemiol. 2019 Aug;61:133–8.
8. Ma Y, Li MD. Establishment of a Strong Link Between Smoking and Cancer Pathogenesis through DNA Methylation Analysis. Sci Rep. 2017 May 12;7(1):1811.
9. Yu L, Ke J, Du X, Yu Z, Gao D. Genetic characterization of thymoma. Sci Rep. 2019 Feb 20;9(1):2369.
10. Dai X, Hua L, Chen Y, Wang J, Li J, Wu F, et al. Mechanisms in hypertension and target organ damage: Is the role of the thymus key? (Review). Int J Mol Med [Internet]. 2018 Mar 30 [cited 2022 Aug 3]; Available from: http://www.spandidos-publications.com/10.3892/ijmm.2018.3605
11. Xue L, Wang L, Dong J, Yuan Y, Fan H, Zhang Y, et al. Risk factors of myasthenic crisis after thymectomy for thymoma patients with myasthenia gravis†. European Journal of Cardio-Thoracic Surgery. 2017 Oct 1;52(4):692–7.
12. Yang H, Youm YH, Vandanmagsar B, Rood J, Kumar KG, Butler AA, et al. Obesity accelerates thymic aging. Blood. 2009 Oct 29;114(18):3803–12.
13. Harrington KA, Kennedy DS, Tang B, Hickie C, Phelan E, Torreggiani W, et al. Computed tomographic evaluation of the thymus-does obesity affect thymic fatty involution in a healthy young adult population? Br J Radiol. 2018 Sep;91(1089):20170609.
14. Liu XD, Shao MR, Sun L, Zhang L, Jia XS, Li WY. Influence of body mass index on postoperative complications after thymectomy in myasthenia gravis patients. Oncotarget. 2017 Jul 12;8(55):94944–50.
15. Carter BW, Betancourt SL, Benveniste MF. MR Imaging of Mediastinal Masses. Topics in Magnetic Resonance Imaging. 2017 Aug;26(4):153–65.
16. Gentili F, Pelini V, Lucii G, Luzzi L, Mazzei FG, Fausto A, et al. Update in diagnostic imaging of the thymus and anterior mediastinal masses. Gland Surg. 2019 Sep;8(S3):S188–207.
17. Thiryayi SA, Rana DN, Narine N, Najib M, Bailey S. Establishment of an endobronchial ultrasound-guided transbronchial fine needle aspiration service with rapid on-site evaluation: 2

years experience of a single UK centre. Cytopathology. 2016 Oct;27(5):335–43.
18. Chira RI, Chira A, Mircea PA, Valean S. Mediastinal masses—transthoracic ultrasonography aspects. Medicine. 2017 Dec;96(49):e9082.
19. Lee HN, Yun SJ, Kim JI, Ryu CW. Diagnostic outcome and safety of CT-guided core needle biopsy for mediastinal masses: a systematic review and meta-analysis. Eur Radiol. 2020 Jan;30(1):588–99.
20. Bian D, Zhou F, Yang W, Zhang K, Chen L, Jiang G, et al. Thymoma size significantly affects the survival, metastasis and effectiveness of adjuvant therapies: a population based study. Oncotarget. 2018 Jan 23;9(15):12273–83.
21. Amini A, Rusthoven CG. Thymoma: does tumor size matter? J Thorac Dis. 2019 Sep;11(Suppl 15):S2005–7.
22. Li WWL, van Boven WJP, Annema JT, Eberl S, Klomp HM, de Mol BAJM. Management of large mediastinal masses: surgical and anesthesiological considerations. J Thorac Dis. 2016 Mar;8(3):E175–84.
23. Kunacheewa C, Wongwiangjunt S, Sukpanichnant S. Concurrent myasthenia gravis-related cervical thymoma in a patient with diffuse large B-cell lymphoma: a case report. J Med Case Rep. 2022 Jan 12;16:10.
24. Mizrahi N, Kugler E, Hayman L, Yeshurun M, Grossman A, Raanani P, et al. T-Lymphoblastic Leukemia/Lymphoma and Thymoma: A Case Report and Review of the Literature of a Rare Association. AHA. 2022;145(1):106–11.
25. Biswas S, Shankar SH, Ray A, Ramteke P. Lymphoma versus thymoma: A diagnostic challenge. Drug Discov Ther. 2020 Nov 4;14(5):249–51.
26. Park HO, Kim SH, Moon SH, Yang JH, Kang DH, Lee JH. Ectopic Cervical Thymoma: A Case Report and Review. Korean J Thorac Cardiovasc Surg. 2017 Aug;50(4):312–5.
27. Welsh JS, Wilkins KB, Green R, Bulkley G, Askin F, Diener-West M, et al. Association between thymoma and second neoplasms. JAMA. 2000 Mar 1;283(9):1142–3.
28. Nishioka R, Nakajima S, Morimoto Y, Suzuki H, Nakamura H, Suzuki M. T-Cell Acute Lymphoblastic Leukemia with Transient Pure Red Cell Aplasia Associated with Myasthenia Gravis and Invasive Thymoma. Internal Medicine. 1995;34(2):127–30.